

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 16:15:03 ON 19 MAY 2005

L1 66 S ZONE 3 NECROSIS
L2 32629 S HEPATOTOXICITY
L3 505 S EXPRESSION MARKER
L4 0 S L1 (S) L3
L5 0 S L1 (P) L3
L6 0 S L1 (S) EXPRESSION
L7 1 S L1 (S) MARKER
L8 0 S L1 (S) GENE
L9 0 S L1 (P) GENE
L10 1 S L2 (S) L3
L11 1 S L2 (P) L3
L12 524 S L2 (S) EXPRESSION
L13 260 S L2 (S) MARKER
L14 20 S L13 (S) GENE
L15 15 DUP REM L14 (5 DUPLICATES REMOVED)
L16 0 S TOXMARKER
L17 0 S L1 (S) ARRAY
L18 250683 S (MICRO-ARRAY) OR (ARRAY)
L19 0 S L1 (P) L18
L20 0 S L2 (P) L19
L21 166 S L2 AND L18
L22 112 S L2 (P) L18
L23 28 S L2 (S) L18
L24 12 DUP REM L23 (16 DUPLICATES REMOVED)

AU Kato, Shinzo
SO Nippon Shokakibyo Gakkai Zasshi (1985), 82(9), 2074-81
CODEN: NIPAA4; ISSN: 0369-4259
TI Experimental study on the significance of serum alcohol dehydrogenase activity
AB An increase in serum alc. dehydrogenase (ALD) activity in rats is a sensitive indicator of hepatic zone 3 necrosis (induced with PhBr, alc., or hypoxia); the increase in serum ALD preceded that of serum glutamate dehydrogenase.

IN Mendrick, Donna; Porter, Mark; Johnson, Kory; Higgs, Brandon; Castle, Arthur; Orr, Michael S.; Elashoff, Michael
SO PCT Int. Appl., 1071 pp.
CODEN: PIXXD2
TI Primary rat hepatocyte toxicity modeling using changes in gene expression as toxicity markers
AB Global changes in patterns of gene expression in response to intoxication with known toxins are identified in rat. The genes and their encoded proteins may be used as toxicity markers in drug screening and toxicity assays. The invention also includes a database of genes and/or proteins characterized by toxin-induced differential expression.

AU Harries H M; Fletcher S T; Duggan C M; Baker V A
SO Toxicology in vitro : an international journal published in association with BIBRA, (2001 Aug-Oct) 15 (4-5) 399-405.
Journal code: 8712158. ISSN: 0887-2333.
TI The use of genomics technology to investigate gene expression changes in cultured human liver cells.
AB The field of genomics has great potential in toxicology; however, the technology is still in its infancy and there are many questions that need to be addressed. In this study we focus on the use of toxicogenomics for the determination of gene expression changes associated with hepatotoxicity. The human hepatoma cell line HepG2 was used to assess the toxic effects of two well-studied hepatotoxins, carbon tetrachloride (CCl₄) and ethanol (EtOH). Replicate dishes of HepG2 cells were exposed to two concentrations of CCl₄ and EtOH--doses which caused 20% and 50% cell death (as determined by the MTT assay) were chosen [0.18% and 0.4% (v/v) CCl₄; 2.5% and 5% (v/v) EtOH] and the cells exposed for periods of 2 and 24 h. mRNA was extracted and used to probe Atlas Human Toxicology II arrays (Clontech). Preliminary data revealed that following a 2-h exposure at the low doses of both compounds, few changes in gene expression were detected. However, after 24-h exposure of the cells to the same low concentration of both compounds, multiple changes in gene expression were observed, many of which were specific to the individual

hepatotoxins, presumably reflecting their different mechanisms of action. CCl₄ treatment of HepG2 cells gave rise to treatment specific up-regulation of genes involved in extracellular transport and cell signalling, whereas EtOH treatment gave rise predominantly to down-regulation of genes involved in stress response and metabolism. In addition, changes in regulation of certain genes (involved in stress response and cell cycle) were common to both treatments. Exposure of HepG2 cells to higher doses of the hepatotoxins gave rise to more changes in gene expression at lower exposure times. These results strongly suggest that different mechanisms of hepatotoxicity may be associated with specific patterns of gene expression, while some genes associated with common cellular responses may be useful as early markers of toxicity.

- AU de Longueville, Francoise; Surry, Dominic; Meneses-Lorente, Georgina; Bertholet, Vincent; Talbot, Valerie; Evrard, Stephanie; Chandelier, Nathalie; Pike, Andrew; Worboys, Phil; Rasson, Jean-Paul; Le Bourdelles, Beatrice; Remacle, Jose
- SO Biochemical Pharmacology (2002), 64(1), 137-149
CODEN: BCPA6; ISSN: 0006-2952
- TI Gene expression profiling of drug metabolism and toxicology markers using a low-density DNA microarray
- AB DNA microarrays are useful tools to study changes of gene expression in response to a treatment with drugs. Here, we describe the optimization of conditions for the cDNA synthesis and hybridization protocols to be used for a low-d. DNA microarray called 'Rat HepatoChips'. This DNA microarray with 59 carefully selected genes could be used to study changes in gene expression levels due to a treatment with xenobiotic. These 59 genes (including 8 housekeeping genes) have been selected among potential toxic markers involved in basic cellular processes and drug metab. related genes. Using the optimized conditions, the results were shown to be reproducible, with 6% variation between the duplicated spots and 10% between arrays. Conditions were optimized to allow quantification with a dynamic range of four log units. In order to demonstrate the major advantage of these tool for studying gene expression, samples of control rat liver were compared with those of animals dosed with phenobarbital (PB) or pregnenolone-16.alpha.-carbonitrile (PCN), two compds. well known to induce cytochrome P 450 isoforms of 2B and 3A subfamilies, resp. This microarray has shown that other genes apart from the corresponding CYP P 450 genes have been changed due to PB and PCN treatment. Apoptosis-related genes have shown to be changed due to PB and PCN treatment, which confirms results from previous work.
- AU Mendrick, D. [Reprint Author]; Higgs, B. W. [Reprint Author]; Porter, M. W. [Reprint Author]; Castle, A. L. [Reprint Author]; Orr, M. S. [Reprint Author]
- SO Toxicological Sciences, (March 2003) Vol. 72, No. S-1, pp. 244. print. Meeting Info.: 42nd Annual Meeting of the Society of Toxicology. Salt Lake City, Utah, USA. March 09-13, 2003. Society of Toxicology. ISSN: 1096-6080 (ISSN print).
- TI Using gene markers identified from a large database built with primary rat hepatocytes for prediction of human hepatotoxicity.
- IN Cunningham, Mary Jane; Kaser, Matthew R.
- SO U.S. Pat. Appl. Publ., 28 pp.
CODEN: USXXCO
- TI Gene expression profiles and identification of toxicity markers for molecular hepatotoxicology modeling
- AB The present invention is based on the elucidation of the global changes in gene expression and the identification of toxicity markers in rat and human liver tissues or cells exposed to a known toxin. Gene expression profiles are provided in response to the known toxins: acetaminophen, benzo[a]pyrene, clofibrate, .alpha.-naphthylisothiocyanate, 4-acetylaminofluorene, hydrazine, fenofibrate, and carbon tetrachloride. The genes may be used as toxicity markers in drug screening and toxicity assays, where hepatotoxicity is assocd. with at least one liver disease pathol. selected from the group consisting of biliary cirrhosis, X-linked adrenoleukodystrophy, Zellweger syndrome, hepatorenal syndrome, hepatitis, and hepatocarcinoma. The invention includes a database of genes characterized by liver toxin-induced differential expression that is designed for use with microarrays and

other solid-phase probes.

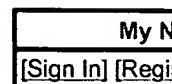
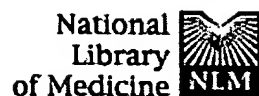
- AU Schuppe-Koistinen Ina; Frisk Anna-Lena; Janzon Lars
SO Toxicology, (2002 Oct 15) 179 (3) 197-219.
Journal code: 0361055. ISSN: 0300-483X.
- TI Molecular profiling of hepatotoxicity induced by a aminoguanidine
carboxylate in the rat: gene expression profiling.
- AB The hepatotoxicity of the aminoguanidine carboxylate
2-[1-[hydrazino(imino)methyl]hydrazino]acetic acid was characterized using
oligonucleotide micro arrays, with the goal to select
compounds from the same class with lower toxicity potential. The approach
included a 14-day repeated- and a single-dose study in the rat as well as
in vitro studies. Common gene expression changes could be followed from
in vivo to in vitro studies. Anyhow, comparing the in vivo and in vitro
response of the compound on gene expression, significant discrepancies
were detected. Many of the genes whose mRNA levels were
increased/decreased in the livers of the animals treated with toxic doses
of the compound, were expressed at higher/lower levels in control
hepatocytes than in control liver. The expression of the majority of
these genes was not affected by in vitro treatment. These data question
the use of gene expression analysis as a marker for drug response in vitro
and illustrate the need of a careful characterization of in vitro systems.
The results presented show that array-based gene expression analysis can
lead to a better understanding of the molecular basis of drug-induced
liver injury and, potentially, be used in the selection process for
compounds and in the design of safer drugs.
- AU Hamadeh Hisham K; Knight Brian L; Haugen Astrid C; Sieber Stella; Amin
Rupesh P; Bushel Pierre R; Stoll Raymond; Blanchard Kerry; Jayadev
Supriya; Tennant Raymond W; Cunningham Michael L; Afshari Cynthia A;
Paules Richard S
SO Toxicologic pathology, (2002 Jul-Aug) 30 (4) 470-82.
Journal code: 7905907. ISSN: 0192-6233.
- TI Methapyrilene toxicity: anchorage of pathologic observations to gene
expression alterations.
- AB Methapyrilene (MP) exposure of animals can result in an array of
adverse pathological responses including hepatotoxicity. This
study investigates gene expression and histopathological alterations in
response to MP treatment in order to 1) utilize computational approaches
to classify samples derived from livers of MP treated rats based on
severity of toxicity incurred in the corresponding tissue, 2) to
phenotypically anchor gene expression patterns, and 3) to gain insight into
mechanism(s) of methapyrilene hepatotoxicity. Large-scale differential
gene expression levels associated with the exposure of male Sprague-Dawley
rats to the rodent hepatic carcinogen MP for 1, 3, or 7 days after daily
dosage with 10 or 100 mg/kg/day were monitored. Hierarchical clustering
and principal component analysis were successful in classifying samples in
agreement with microscopic observations and revealed low-dose effects that
were not observed histopathologically. Data from cDNA microarray analysis
corroborated observed histopathological alterations such as hepatocellular
necrosis, bile duct hyperplasia, microvesicular vacuolization, and portal
inflammation observed in the livers of MP exposed rats and provided
insight into the role of specific genes in the studied toxicological
processes.
- AU Coen Muireann; Ruepp Stefan U; Lindon John C; Nicholson Jeremy K; Pognan
Francois; Lenz Eva M; Wilson Ian D
SO Journal of pharmaceutical and biomedical analysis, (2004 Apr 1) 35 (1)
93-105.
Journal code: 8309336. ISSN: 0731-7085.
- TI Integrated application of transcriptomics and metabonomics yields new
insight into the toxicity due to paracetamol in the mouse.
- AB Gene chip array (Affymetrix) data from liver tissue and high
resolution 1H NMR spectra from intact liver tissue, tissue extracts and
plasma have been analyzed to identify biochemical changes arising from
hepatotoxicity in mice dosed with acetaminophen. These data sets
have been co-interpreted in terms of common metabolic pathways. The
principal metabolic changes comprised a decrease in hepatic glucose and
glycogen in intact tissue, coupled with an increase in lipid content, with
increases in the levels of glucose, pyruvate, acetate and lactate in
plasma, and increases in alanine and lactate in the aqueous tissue
extracts. Collectively these data provide evidence for an increased rate

of hepatic glycolysis. The metabolic observations were consistent with the altered levels of gene expression relating to lipid and energy metabolism in liver which both preceded and were concurrent with the metabolic perturbations. The results show that these two technology platforms together offer a complementary view into cellular responses to toxic processes, providing new insight into the toxic consequences, even for well-studied therapeutic agents such as acetaminophen.

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	1625	hepatotoxicity	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 14:44
L2	0	l1 near5 (expression adj marker)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 14:44
L3	0	l1 with (expression adj marker)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 14:44
L4	0	l1 same (expression adj marker)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 14:44
L5	98	l1 same expression	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 14:45
L6	20	l1 near5 expression	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 14:48
L7	377	liver adj necrosis	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 14:48
L8	2	l7 near5 expression	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 14:48
S1	0	denise near mccabe.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 12:02
S2	22	oswald near crasta.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/18 17:36
S3	1	darius near dziuda.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/18 17:35
S4	0	craig near hyde.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/18 17:35
S5	2	robert near gerwien.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/18 17:35

S6	8	S2 and necrosis	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/18 17:37
S7	1	09/264,807	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/18 17:38
S8	0	bonnie near garrow.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/18 17:38
S9	0	bonnie near2 garrow.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/18 17:39
S10	1	sara near2 mullahy.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/18 17:43
S11	0	09/539,334	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/18 17:44
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S13	17	S12 and endocrine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/18 17:45
S14	611	curagen.as.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 12:05
S15	0	10/663,418	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 12:02
S16	74	S14 and toxic\$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 12:05
S17	17	S14 and zone	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 12:07
S18	21	S14 and necrosis	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 12:08

S19	0	toxmarker	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 12:09
S20	0	(zone) adj "3" adj (necrosis)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 12:10
S21	264	zone near2 necrosis	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 12:11
S22	0	S21 near "3"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 12:11
S23	0	S21 near2 "3"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 12:11
S24	182	zone adj2 necrosis	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 12:11
S25	22	S24 with "3"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/05/19 14:43



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☐ 1: McCabe DP, Presmanes AG, Robertson CL, Smith AD. Related Articles, Links

Item-specific processing reduces false memories.
Psychon Bull Rev. 2004 Dec;11(6):1074-9.
PMID: 15875978 [PubMed - in process]

☐ 2: McCabe DJ, Pereira AC, Clifton A, Bland JM, Brown MM; CAVATAS Investigators. Related Articles, Links

Restenosis after carotid angioplasty, stenting, or endarterectomy in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS).
Stroke. 2005 Feb;36(2):281-6. Epub 2005 Jan 13.
PMID: 15653582 [PubMed - in process]

☐ 3: McCabe D, O'Regan K, Murphy PT. Related Articles, Links

Relationship between cell surface expression of CD38 and of vascular endothelial growth factor in B-cell chronic lymphocytic leukemia.
Leuk Res. 2004 Nov;28(11):1239-40. No abstract available.
PMID: 15380351 [PubMed - indexed for MEDLINE]

☐ 4: McCabe DJ, Harrison P, Sidhu PS, Brown MM, Machin SJ. Related Articles, Links

Circulating reticulated platelets in the early and late phases after ischaemic stroke and transient ischaemic attack.
Br J Haematol. 2004 Sep;126(6):861-9.
PMID: 15352991 [PubMed - indexed for MEDLINE]

☐ 5: Shucard DW, Abara JP, McCabe DC, Benedict RB, Shucard JL. Related Articles, Links

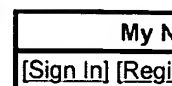
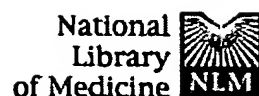
The effects of covert attention and stimulus complexity on the P3 response during an auditory continuous performance task.
Int J Psychophysiol. 2004 Nov;54(3):221-30.
PMID: 15331213 [PubMed - indexed for MEDLINE]

☐ 6: Bennett DL, McCabe DJ, Stevens JM, Mifsud V, Kitchen ND, Giovannoni G. Related Articles, Links

Tumefactive neuro-Behcet disease.
Neurology. 2004 Aug 24;63(4):709. No abstract available.
PMID: 15326247 [PubMed - indexed for MEDLINE]

☐ 7: Beekey MA, McCabe DJ, Marsden JE. Related Articles, Links

Zebra mussels affect benthic predator foraging success and habitat choice on soft sediments.



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☐ 1: [Crasta OR, Folkerts O.](#)[Related Articles, Links](#)

Open architecture expression profiling of plant transcriptomes and gene discovery using GeneCalling technology.

Methods Mol Biol. 2003;236:381-94.

PMID: 14501077 [PubMed - indexed for MEDLINE]

☐ 2: [Hu X, Bidney DL, Yalpani N, Duvick JP, Crasta O, Folkerts O, Lu G.](#) [Related Articles, Links](#)

Overexpression of a gene encoding hydrogen peroxide-generating oxalate oxidase evokes defense responses in sunflower.

Plant Physiol. 2003 Sep;133(1):170-81.

PMID: 12970484 [PubMed - indexed for MEDLINE]

☐ 3: [Mysore KS, Crasta OR, Tuori RP, Folkerts O, Swirsky PB, Martin GB.](#) [Related Articles, Links](#)

Comprehensive transcript profiling of Pto- and Prf-mediated host defense responses to infection by Pseudomonas syringae pv. tomato.

Plant J. 2002 Nov;32(3):299-315.

PMID: 12410809 [PubMed - indexed for MEDLINE]

☐ 4: [Simmons CR, Grant S, Altier DJ, Dowd PF, Crasta O, Folkerts O, Yalpani N.](#) [Related Articles, Links](#)

Maize rhm1 resistance to Bipolaris maydis is associated with few differences in pathogenesis-related proteins and global mRNA profiles.

Mol Plant Microbe Interact. 2001 Aug;14(8):947-54.

PMID: 11497466 [PubMed - indexed for MEDLINE]

☐ 5: [Bruce W, Desbons P, Crasta O, Folkerts O.](#) [Related Articles, Links](#)

Gene expression profiling of two related maize inbred lines with contrasting root-lodging traits.

J Exp Bot. 2001 Mar;52(Spec Issue):459-68.

PMID: 11326052 [PubMed - indexed for MEDLINE]

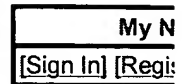
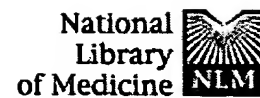
☐ 6: [Crasta OR, Francki MG, Bucholtz DB, Sharma HC, Zhang J, Wang RC, Ohm HW, Anderson JM.](#) [Related Articles, Links](#)

Identification and characterization of wheat-wheatgrass translocation lines and localization of barley yellow dwarf virus resistance.

Genome. 2000 Aug;43(4):698-706.

PMID: 10984183 [PubMed - indexed for MEDLINE]

☐ 7: [Xu W, Subudhi PK, Crasta OR, Rosenow DT, Mullet JE, Nguyen HT.](#) [Related Articles, Links](#)



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Specialized PC software package for creation of computer systems supporting partial diagnostics based on numerical results of medical examinations.

Med Inform (Lond). 1990 Oct-Dec;15(4):319-26.

PMID: 2277555 [PubMed - indexed for MEDLINE]

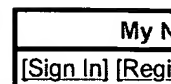
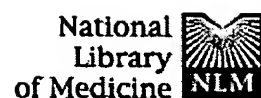
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☐ 1: [Terada I, Hyde C.](#)[Related Articles, Links](#)

Establishing nephrology nursing specialization in Japan: a matter of urgency.

EDTNA ERCA J. 2004 Oct-Dec;30(4):234-7.

PMID: 15835418 [PubMed - in process]

☐ 2: [Fishbein DH, Eldreth DL, Hyde C, Matochik JA, London ED, Contoreggi C, Kurian V, Kimes AS, Breeden A, Grant S.](#)[Related Articles, Links](#)

Risky decision making and the anterior cingulate cortex in abstinent drug abusers and nonusers.

Brain Res Cogn Brain Res. 2005 Apr;23(1):119-36.

PMID: 15795139 [PubMed - in process]

☐ 3: [Willis BH, Barton P, Pearmain P, Bryan S, Hyde C.](#)[Related Articles, Links](#)

Cervical screening programmes: can automation help? Evidence from systematic reviews, an economic analysis and a simulation modelling exercise applied to the UK.

Health Technol Assess. 2005 Mar;9(13):1-222.

PMID: 15774236 [PubMed - in process]

☐ 4: [Fishbein D, Hyde C, Eldreth D, London ED, Matochik J, Ernst M, Isenberg N, Steckley S, Schech B, Kimes A.](#)[Related Articles, Links](#)

Cognitive performance and autonomic reactivity in abstinent drug abusers and nonusers.

Exp Clin Psychopharmacol. 2005 Feb;13(1):25-40.

PMID: 15727501 [PubMed - indexed for MEDLINE]

☐ 5: [Song FJ, Fry-Smith A, Davenport C, Bayliss S, Adi Y, Wilson JS, Hyde C.](#)[Related Articles, Links](#)

Identification and assessment of ongoing trials in health technology assessment reviews.

Health Technol Assess. 2004 Nov;8(44):iii, 1-87. Review.

PMID: 15525479 [PubMed - indexed for MEDLINE]

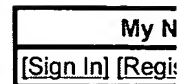
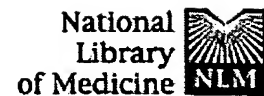
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